

Notice of Allowability

Application No.

09/921,819

Examiner

Anne Marie S. Wehbe

Applicant(s)

BUELOW ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the amendment filed on 5/9/06.
2. ☒ The allowed claim(s) is/are 17-20,22-30,67 and 69-72.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

EXAMINER'S AMENDMENT

Applicant's amendment and response received on 5/9/06 have been entered. Claims 1-16, 21, 31-66, 68, and 73-76 are canceled. Claims 17-20, 22-30, 67, and 69-72 are pending.

Following entry of this examiner's amendment, the rejection of the claims under 35 U.S.C. 102 and 103 are withdrawn, see the Reasons for Allowance below for a detailed discussion. Claims 17-20, 22-30, 67, and 69-72 are considered allowed.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ginger Dreger on 5/22/06.

The application has been amended as follows:

- 1) In claim 19, line 2, the word "one" has been replaced by the word -- two --.
- 2) In claim 24, line 2, the word "one" has been replaced by the word -- two --.

3) Claim 27 has been rewritten as follows:

Claim 27. A method of making a transgenic vector comprising a humanized Immunoglobulin (Ig) locus capable of producing a functional repertoire of humanized antibodies in a non-human animal generating antibody diversity primarily through gene conversion and/or hypermutation, comprising:

- (i) obtaining a DNA fragment comprising an Ig locus or a portion therefor from said non-human animal, which comprises at least two V gene segments, at least one J gene segment and at least one constant region gene segment, and non-coding sequences; and
- (ii) integrating by homologous recombination at least one functional human V gene segment encoding a human V region amino acid sequence, into said DNA fragment of step (i) to produce a humanized Ig locus,

wherein the V gene segments present are separated only by non-coding, non-human sequences derived from said non-human animal that generates antibody diversity primarily through gene conversion and/or hypermutation, and at least one of the functional V gene segments encoding a human V region amino acid sequence is placed downstream of the other V gene segments, and

wherein said Ig gene segments are juxtaposed in an unarranged, partially rearranged or fully rearranged configuration, as to permit gene rearrangement and gene conversion of said humanized Ig locus and the production of a functional repertoire of humanized antibodies with V region amino acid sequences encoded by more than one V region gene segment, in said non-human animal.

4) In claim 28, line 2, the words “is achieved” are deleted; and further in line 2, the phrase “, thereby replacing” is replaced by the word -- replaces --.

5) In claim 30, the word “franking” is replaced by the word -- flanking --.

6) Claim 67 has been rewritten as follows:

Claim 67. A transgenic vector comprising a humanized Immunoglobulin (Ig) locus, wherein

- (a) said humanized Ig locus comprises multiple Ig gene segments, including multiple variable (V) gene segments, multiple J gene segments, and one or more constant region gene segments,
- (b) at least one of said gene segments is a functional V gene segment encoding a human V region amino acid sequence,
- (c) said V gene segments are separated only by non-coding, non-human sequences derived from a non-human animal that generates antibody diversity primarily through gene conversion and/or hypermutation,
- (d) at least one of said functional V gene segments encoding a human V region amino acid sequence is placed downstream of the other V gene segments, and
- (e) said Ig gene segments are juxtaposed in an unarranged, partially rearranged or fully rearranged configuration, and

wherein, as a result of structural features (a)-(e), said humanized Ig locus is capable of undergoing gene conversion and producing a repertoire of humanized immunoglobulins with V region amino acid sequences encoded by segments of more than one V region gene, in said non-human animal.

7) In the specification on page 9, line 6, -- **(a-d)** -- is inserted after "Figure 1".

8) In the specification on page 9, line 10, -- **(a-e)**-- is inserted after "Figure 2".

9) In the specification on page 9, line 13, -- **(a-b)**-- is inserted after "Figure 3".

The following is an examiner's statement of reasons for allowance: the claims as amended by this examiner's amendment are free of the prior art of record, and specifically the teachings of Lonberg et al. and Fell et al. for the following reasons. The vectors taught by Lonberg contain multiple human V region gene segments. However, while Lonberg does teach to insert non-human regulatory sequences in the vector, Lonberg does not teach that each of the human V region gene segments is separated by only non-human coding sequences. Further, while Fell teaches homologous recombination to replace either a non-human Ig V gene segment or C gene segment with the corresponding human gene segment, Fell primarily teaches that recombination is between the chromosome and a replacement vector, not an isolated Ig locus and a replacement vector. In addition, the sole teachings for homologous recombination with isolated

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DNA in Fell are directed to recombination into an isolated rearranged immunoglobulin gene that does not comprise more than one V region gene segment. Therefore, as the instant claims are limited to vectors comprising more than one non-human V region gene segment and at least one human V region gene segment and which further comprise only non-human non-coding sequences between the V region gene segments, the prior art of record neither anticipates nor renders obvious the claimed invention.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

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Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'A. Wehbe', with a long horizontal flourish extending to the right.